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TRANSMITTAL OF APPEAL BRIEF (Large Entity)

Docket No.
NOV-0001

In re Application Of:
Sophie Chen

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
10/072,823	02/08/2002	M.V. Meller	23413	1654	1435

Invention:

COMMISSIONER FOR PATENTS:

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Karen A. LeCuyer
Signature

Dated: **November 29, 2004**

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Michelle E. Fetzner
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Michelle E. Fetzner
Typed or Printed Name of Person Mailing Correspondence

cc:

Docket No. NOV-0001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	CHEN	)
		) Before the Board of Appeals
SERIAL NUMBER:	10/072,823	)
		)
FILED:	February 8, 2002	) Appeal No.:
		)
FOR:	ANTI-CANCER AGENTS AND METHOD OF USE THEREOF	)

APPEAL BRIEF

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I. REAL PARTY IN INTEREST

The real party in interest in this appeal is Sophie Chen.

II. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences known to Appellant, Appellant's legal representatives, or assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

Claims 1-9, 11-16, 18-23, 26-29, and 32-35 are pending in the application. All of the pending claims stand rejected. The rejection of claims 1-9, 11-16, 18-23, 26-29, and 32-35 is appealed.

IV. STATUS OF AMENDMENTS

There have been no amendments filed subsequent to receipt of the Final Office Action dated July 28, 2004.

V. SUMMARY OF THE INVENTION

The present invention relates to compositions suitable for treatment of cancer such as prostate, breast, colon, lung, and bladder cancers. The compositions comprise compounds from various plant sources that may be extracts found naturally in the plant, or that may be synthesized and/or altered by pharmaceutical means. (Page 6, lines 5-7) The extracts include compounds such as oridonin, lupulone, bavachin, bavachalcone, bavachinin, bavachromene, gensenoside, baicalin, soy flavonoid, soy isoflavonoid, curcumin, pharmaceutically acceptable salts or esters, selectively substituted analogs, and combinations comprising at least one of the foregoing compounds. (Page 6, lines 12-16) Administration of compounds such as oridonin, lupulone, bavachin, bavachalcone, bavachinin, and bavachromene is effective to have anti-prostate cancer, anti-breast cancer, anti-colon cancer, anti-lung cancer, or anti-bladder cancer activity *in vivo*. (Page 11, lines 4-10) The compounds and/or plant extracts may be formulated as pharmaceutically acceptable compositions.

In the Examples, the isolation and characterization of oridonin from Rabdosia rubescens is described. Oridonin was purified to greater than 95% purity. Lupulone was isolated from Humulus lupulus and purified. The anti-cancer activity of oridonin and lupulone was evaluated by determining their effect on inhibition of cancer cell growth, modulation of the cell cycle, induction of apoptosis, and ability to regulate hormone and cytokine receptors. The cell lines employed in the experiments include LNCaP which is an androgen receptor positive prostate cancer cell line; MCF-7 which is an androgen receptor positive breast cancer cell line; and DU-145 which is an androgen receptor negative prostate cancer cell line. (Page 15, lines 19-23)

LNCaP, DU-145 and MCF-7 cells were grown and the ability of oridonin and lupulone to inhibit cell grown was determined using an MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) assay. MTT allows for the percentage of viable cells to be counted. Figures 1, 2, and 3 demonstrate that both oridonin and lupulone are effective growth inhibitors of both androgen receptor positive cell lines (LNCaP and MCF-7 cell lines), and of androgen receptor negative cell lines (DU-145). They are inhibitors of both breast and prostate cancer cell line growth. Also, the inhibition of cell growth is dose dependent.

The effect of oridonin and lupulone on the cell cycle of different cell types was then studied. The distribution of cells in various stages of the cell cycle were determined by first staining the cells with the DNA specific fluorochrome, and then by measuring cellular DNA content with an ELITE ESP flow cytometer (Coulter Inc., Fl.) using UV laser illumination. Oridonin affects the cell cycle of LNCAP androgen receptor positive prostate cancer cells at the G1 phase while lupulone affects the cell cycle of LNCAP androgen receptor positive prostate cancer cells at the G2M phase and induces a strong apoptosis. Oridonin affects the cell cycle of DU-145 androgen receptor negative cells at the G2M phase. Oridonin affects the cell cycle of MCF-7 breast cancer cells at the S phase and lupulone affects the cell cycle of MCF-7 breast cancer cells at the G1 phase. (Pages 18-21)

The effect of oridonin on suppression or promotion of apoptosis was investigated by examining the effect of oridonin on the Bcl-2 and Bax gene products. It has been demonstrated in the past that the balance between the Bcl-2 and Bax gene products determines the extent to

which apoptosis is suppressed or promoted. To determine the Bcl-2:Bax ratio in oridonin-incubated LNCaP cells, a Western blotting procedure was performed. Flow cytometric measurement was performed to confirm the results obtained by Western blot. As shown in Figure 11, the ratio of Bax/Bcl-2 increased significantly in the presence of oridonin, thereby indicating that oridonin plays a role in up-regulating Bax protein expression, and in down-regulating the Bcl-2 expression. Flow cytometry experiments confirmed this result as approximately a 75% increase in the ratio of Bax/Bcl-2 was obtained in the presence of 8.24 μM oridonin. The concentration ratio of p53 and Bcl-2 proteins obtained from flow cytometric measurement was also used to evaluate the pro-apoptotic property of oridonin on LNCaP cells. A 100% increase in the ratio of p53/Bcl-2 was observed in the presence of 8.24 μM oridonin. (Pages 21-24)

Apoptosis in LNCaP cell lines caused by oridonin exposure was also studied. To determine apoptosis in cells, a quantitative assay for the detection of DNA breakage, using the terminal deoxyribonucleotide transferase (TdT) color reaction assay (TiterTACS, Trevigen, Gaithersburg, MD), was employed. Figure 13 shows a dose-responsive apoptosis of LNCaP induced by oridonin at concentrations of 0, 8.24 μM, and 13.74 μM at 48 hours. About 6% cell apoptosis of LNCaP was induced by oridonin at a concentration of 13.7 μM on the ratio of p53/Bcl-2. A 100% increase was detected. (Pages 24-25)

Overall, the experiments demonstrate that both oridonin and lupulone are effective cell cycle inhibitors. It was further shown in the present application that oridonin down-regulates Bcl-2 and up-regulates Bax and p53, which ultimately leads to an apoptotic cascade in the cancer cells. As such, both oridonin and lupulone complement each other in inducing apoptosis of the targeted cancer cells at various cell cycle stages. The results also show that oridonin and lupulone are effective in inhibiting the cell cycle in both breast cancer and prostate cancer cell lines.

VI. ISSUES

Claims 1-9, 11-16, 18-23, 26-29, and 32-35 stand rejected under 35 U.S.C. § 103 as being allegedly unpatentable over JP 57-167938, GB 1476016, or JP 352102434 taken with JP 11-236334 or JP 52-145509.

VII. GROUPING OF CLAIMS

The claims stand together.

VIII. ARGUMENT

Claims 1-9, 11-16, 18-23, 26-29, and 32-35 are Patentable Under 35 U.S.C. § 103 Over JP 57-167938, GB 1476016, or JP 352102434 Taken With JP 11-236334 or JP 52-145509.

GB 1476016 and JP 52-102434 to Fujita et al. ("Fujita") belong to the same patent family and disclose pharmaceutical compositions comprising oridonin and/or lasiokaurin as antitumor agents. The pharmaceutical compositions are prepared from isolated oridonin and/or lasiokaurin and further comprise a solid or liquid carrier. The anti-tumor activity of the compounds was tested by injecting the compounds into mice containing Erlich ascites tumor cells injected into the peritoneum. Erlich ascites tumor cells are a type of epithelial cell. It is stated that oridonin increased the survival rate of mice having the Erlich ascites tumor cells compared to controls with no injected oridonin. Because lasiokaurin and oridonin have similar chemical structures, it is likely that they have similar biological activity.

JP 57-167938 discloses two new diterpenoids allegedly having carcinostatic activity. The abstract states that oridonin is known to exhibit carcinostatic activity. Carcinostatic activity refers to the ability of oridonin to stop the growth of cancer. There is, however, no teaching as to the types of cancer which may be treated successfully with oridonin. As with the foregoing references, the two new diterpenoids disclosed in this reference are closely related chemicals which may be expected to have similar biological activity.

JP 11-236334 discloses the use of twenty-three plants or their extracts as cell adhesion inhibitors or cancer metastasis inhibitors; the plants include, inter alia, Humulus lupulus. Cancer metastasis inhibitors are compounds that can prevent the spread of cancer from one part of the body to the other. There is, however, no disclosure as to the types of cancer for which the plant extracts act as inhibitors. Furthermore, this patent describe 23 plant extracts as adhesion/metastasis inhibitors and as anti cancer remedies. This reference does not describe the chemical contents of the extracts. In addition, the anti-adhesion and anti-metastasis activity relates only to secondary tumor formation. This reference does not demonstrate the inhibition of the growth of primary tumors.

JP 52-145509 alleges that "a bitter principle of hops of Humulus lupulus," prepared by aqueous extraction of dried hops, exhibits an anti-cancer effect for cancers of the stomach, liver, lung, and breast. This patent discloses only an aqueous extract of Humulus lupulus as the anti cancer preparation. However, there are active components in hops such as lupulone which cannot be extracted by water and can only be extracted by alcohol or organic solvents. Thus, it is not clear if the extract in this reference actually contains lupulone. Furthermore, there is no teaching as to how to isolate specific chemicals from the extract.

Claim 1 is directed to a composition for treating or preventing prostate cancer or breast cancer, comprising oridonin, a pharmaceutically acceptable salt or ester of oridonin, or a selectively substituted analog of oridonin, and lupulone, a pharmaceutically acceptable salt or ester of lupulone, a selectively substituted analog of lupulone, or a combination thereof. The oridonin and lupulone may be in the form of purified chemicals or plant extracts, so long as the plant extracts are purified in such a manner as to contain the claimed compounds. While the cited references appear to suggest the use of oridonin and its closely chemically related analogs, or an extract of Humulus lupulus to treat cancer, these references do not provide the motivation to combine oridonin and lupulone as the Appellant has done. The cited references do not provide the motivation to combine oridonin and lupulone to treat the same types of cancers, let alone breast and prostate cancer. The chemical structure and biological activity of oridonin and lupulone are very different from each other. They are not analogs. It is only the Appellant's own disclosure that provides the motivation to combine

oridonin and lupulone to treat cancer based on the Appellant's study of the biological mechanism of these compounds. The rationale for the Appellant to choose this combination is described below:

First, the antiproliferative activities of oridonin and lupulone were demonstrated in Figures 1 to 3 (cell growth-inhibition) for a prostate cancer cell line, LNCaP, which expresses androgen receptors (AR positive), for a prostate cancer cell line, DU-145, which does not express androgen receptors (AR negative), and for a breast cancer cell line, MCF-7, which also expresses androgen receptors. All three cancer cell lines contain estrogen receptor beta (i.e., ER beta). Therefore, oridonin and lupulone are expected to have anticancer activities for prostate and breast cancer cells.

Second, each of oridonin and lupulone induced apoptosis in prostate cancer cell lines (Figure 5 and amendment submitted Feb. 6, 2004). Thus, mechanistically, both oridonin and lupulone inhibit cancer cell growth by an apoptotic mechanism.

Third, it is shown in the present application that the anticancer activity of lupulone is directed at the inhibition of primary tumor growth. Not only was cancer cell growth inhibited, but the cell cycle of the cancer cells was also modulated at specific points in the cell cycle.

In the absence of data regarding the specificity and mechanism of action of various anticancer agents, it is not obvious which agents can and should be combined. This is at least in part because different anticancer agents have specificity for, and may be used to treat, different forms of cancer. When, as in the present case, the two agents to be combined appear to have specificity for different types of cancer, and have not been shown to be useful to treat the same types of cancer, there is no motivation to combine the two agents. In addition, different anticancer agents act by different mechanisms and may have antagonistic or synergistic effects. Anticancer agents may work, for example, as alkylating agents, topoisomerase I and II inhibitors, RNA/DNA antimetabolites, and antimitotic agents, for example. Thus, even if two anticancer agents are independently effective at treating a particular type of cancer, they may have antagonistic effects which would suggest that they should not be combined.

An Examiner cannot establish obviousness by locating references that describe various

aspects of a patent applicant's invention without also providing evidence of the motivating force which would have impelled one skilled in the art to do what the patent applicant has done. *Ex parte Levengood*, 28 U.S.P.Q.2d 1300 (Bd. Pat. App. Int. 1993). The references, when viewed by themselves and not in retrospect, must suggest the invention. *In Re Skoll*, 187 U.S.P.Q. 481 (C.C.P.A. 1975).

Regarding oridonin, there are three cited references that disclose the use of oridonin. GB 1476016 and JP 52-102434 disclose the use of oridonin to treat Erlich ascites tumor cells, a type of epithelial cell. JP 57-167938 discloses only general carcinostatic activity of oridonin and does not teach the types of cancer for which oridonin has specificity. The cited references do not teach the use of oridonin to treat breast and prostate cancer, only epithelial calls and non-specific anticancer activity. The references also provide no teaching as to the anticancer mechanism of oridonin.

Regarding lupulone, there are two references that teach the use of Humulus Lupulus extract to treat cancer. JP 11-236334 does not teach the types of cancer for which Humulus lupulus extract is a cancer metastasis inhibitor. JP 52-145509 teaches that Humulus lupulus aqueous extract is effective for cancers of the stomach, liver, lung, and breast. Since lupulone can not simply be extracted from aqueous solution (i.e., it dissolves in alcohol), the JP 52-145509 patent does not appear to describe an extract comprising lupulone. As is known to those of skill in the art, the composition of a plant extract is dependent upon the method used to obtain the extract, and particularly on the solvents employed. Thus, it is not clear that these references teach the use of lupulone to treat cancer as it is not certain that the extracts contain lupulone. In addition, these references provide no teaching as to the anticancer mechanism of lupulone.

Based on the references cited by the Examiner, there appears to be no overlap between the cancer-type specificity of oridonin and lupulone. Appellant submits that there is no motivation provided by the references to combine these agents as in the present application.

It is well known in the pharmaceutical arts that different types of cancer respond differently to different anticancer agents. (See, for example, EXHIBIT 1 from the May 7, 2004

amendment, Cell: A Molecular Approach). The type of treatment used to treat cancer depends, in part, on the type of cancer to be treated. (See, for example, EXHIBIT 2, www.bymyside.com/treatment/types_treatment.jsp) Combinations of anticancer agents should be chosen, at least in part, based on the type of cancer to be treated. One of ordinary skill in the art, when designing a combination anticancer therapy, would consider the cancer-type specificity and mechanism of action of each of the individual anticancer agents. Considering that, based on the cited references, oridonin and lupulone have specificity for different types of cancer, one of ordinary skill in the art would not be motivated to combine oridonin and lupulone as the Appellant has done.

The cited references also provide no expectation of success for the combination of oridonin (or salt, ester, or analog thereof) and lupulone (or salt, ester, or analog thereof) recited in Appellant's Claim 1. According to Todd R. Goulb, over the last 25 years "no new drugs have entered standard treatment protocols; rather it has been the optimization of combinations of old drugs, based entirely on clinical empiricism and trial and error". (EXHIBIT 3, May 7, 2004 amendment, Mining the genome for combination therapies) This statement suggests that optimization of drug combinations is not straightforward and in fact requires "clinical empiricism and trial and error". In fact, certain combinations of anticancer agents can have antagonistic effects. For example, antimitotic agents such as paclitaxel and G_1-S arresting agents such as 5-fluorouracil have antagonistic effects. (Johnson et al. Clinical Cancer Research 5, 2559-2565, 1999, EXBIBIT 4, May 7, 2004 amendment) In this case, the G_1-S arresting agent interfered with the ability of the antimitotic agent to induce apoptotic cell death. Thus, without some knowledge of the mechanism of action of the particular anti-cancer agents and/or clinical data, one of ordinary skill in the art would not simply combine any two anti-cancer agents.

In the Advisory Action dated July 28, 2004, the Examiner states "The references just happen to teach that the individual components can be used to treat cancer. This in and of itself would have motivated one of ordinary skill in the art to use the two components together to produce the same composition as claimed". (Page 2)

Appellant strongly disagrees. As explained above, one of ordinary skill in the art would not combine any two anticancer agents absent information regarding the cancer specificity and/or mechanism of action of the agent. Anticancer activity of compounds alone is not sufficient motivation to combine compounds, and does not provide an expectation of success for the combination. First, there is no teaching in the cited references that oridonin and lupulone are effective to treat the same types of cancers. Second, there is no teaching in the references that the two compounds have compatible biological mechanisms. For at least these reasons, one of ordinary skill in the art would not be motivated to do what the Appellant has done.

The present application, in contrast to the cited references, provides ample support for the use of a combination of oridonin and lupulone to treat breast and prostate cancer. As shown in the Examples of the present application, oridonin affects the cell cycle of LNCAP androgen receptor positive prostate cancer cells at the G1 phase; it affects the cell cycle of DU-145 androgen receptor negative cells at the G2M phase; and it affects the cell cycle of MCF-7 breast cancer cells at the S phase. Lupulone affects the cell cycle of LNCAP androgen receptor positive prostate cancer cells at the G2M phase and induces a strong apoptosis; and it affects the cell cycle of MCF-7 breast cancer cells at the G1 phase. It was further shown in the present application that oridonin down-regulates Bcl-2 and up-regulates Bax and p53, which ultimately leads to an apoptotic cascade in the cancer cells. As such, both oridonin and lupulone complement each other in inducing apoptosis of the targeted cancer cells at various cell cycle stages.

It has thus been shown by the Appellant that oridonin and lupulone affect prostate and breast cancer cells by affecting the cell cycle in a similar manner. Based on the Appellant's data, it is not expected that oridonin and lupulone will have antagonistic effects, and in fact, they may have synergistic effects. Thus, Appellant has demonstrated that oridonin and lupulone may be combined to treat prostate and breast cancer.

In making the rejection, the Examiner states "Applicant has argued that the components of the claimed composition are not taught in the references as being extracts but it is clear from

the references themselves that they are from plants making them plant extracts by definition". (February 9, 2004 Office Action, Page 2) Applicant believes the Examiner is referring to the statement in the November 2003 Amendment with RCE that "JP 57167938, GP1476016, and JP 352102434, describe the use of isolated compounds and therefore teach away from the use of oridonin-containing extracts". Applicants concede that JP 57167938, GP1476016, and JP 3521024 teach compounds isolated from plants, however, Applicants would characterize these isolates as isolated compounds and not as plant extracts because these extracts appear to be substantially pure. Support for this interpretation can be found, for example, in GP1476016 where the use of the isolated effective components (i.e., oridonin and lasaiokaurin) is distinguished from the compounds in "compounded or impure form", i.e., an extract. Similarly, JP 57167938 describes the purification of oridonin from a plant extract. Thus, the references for oridonin do not describe the use of crude plant extracts, but instead describe the use of oridonin which has been isolated from a crude plant extract. These references are distinctly different from the references cited for lupulone in which an extract from Humulus lupulus is described, with no indication given that any components, let alone lupulone, were purified from the extract. Thus, when the references are considered as a whole – as they must be – the different forms of the respective compositions teach away from the suggested combination of references. One of ordinary skill in the art would not combine a purified compound (i.e., oridonin) with a crude extract (i.e., an extract of Humulus lupulus) as suggested by the Examiner. Thus, there is no motivation to combine the references.

The Examiner further states "Applicant argues that the Examiner has not considered their argument concerning expectation of success but the fact of the matter is that all the references each teach that oridonin and lupulone are known in the art individually to be used as anti-cancer/carcinostatic agents". (February 9, 2004 Office Action, Page 2) As explained in detail above, the mere disclosure that two agents have some anticancer activity does not provide the motivation to combine the agents, especially when the two agents belong to different chemical classes with different biological activity. In fact, depending on the mechanism of action of the two anticancer agents, the agents may well have antagonistic effects. Further, the disclosure of an agent for the treatment of one type of cancer is not sufficient to suggest that the agent is

suitable to treat other types of cancer. Depending upon the type of cancer and the mechanism of action of the particular anticancer agents, some agents may be combined, while others would not and should not be combined. The cited references do not teach the use of oridonin and lupulone to treat the same types of cancer nor do they teach the mechanism of action of oridonin and lupulone. Further, the references do not provide any motivation to combine oridonin and lupulone. Thus, the Examiner's statement regarding expectation of success is not understood. Appellant maintains that the references themselves do not provide an expectation of success for the combination of oridonin and lupulone.

Regarding JP 11-236334, the Examiner states that Applicant argues that "Humulus lupulus is only one of a number of extracts listed but the reference very clearly states that Humulus lupulus is used and can be used". (February 9, 2004 Office Action, Page 2) Applicants maintain that JP 11-236334 discloses a large number of plant extracts having utility as cancer metastasis inhibitors, but not antiproliferative or apoptosis inducing agents. There is no motivation in JP 11-236334 to combine any of the disclosed plant extracts with other anticancer agents. Further, there is no motivation to select Humulus lupulus over any other of the plant extracts listed in the reference to combine with any other anti-cancer agent, let alone oridonin.

Lastly, the Examiner states regarding the previously cited case law "These cases are routinely used in pharmaceutical arts and this case involves a plant extract which does not need FDA approval, so technically it is a natural pharmaceutical not as applicant has suggested". (February 9, 2004 Office Action, Page 2) Appellant does not understand this comment, particularly the Examiner's reference to the FDA. Appellant is seeking a patent, not FDA approval. Further, Appellant is claiming a composition "wherein the composition is suitable for the treatment or prevention of prostate cancer and breast cancer". Whether a "natural pharmaceutical" or a "non-natural pharmaceutical" Appellant maintains that a composition suitable for the treatment of various cancers is a pharmaceutical composition. Similar to synthetic pharmaceuticals, the development of natural pharmaceuticals also requires an effort to conduct laboratory research and obtain proprietary knowledge. It is well-established that the pharmaceutical arts are highly unpredictable. The references cited by the Examiner are not

particularly relevant to the unpredictable pharmaceutical arts. *In re Pinten*, 459 F.2d 1053, 173 USPQ 801 (C.C.P.A. 1972)(relating to a combination of surfactants); *In re Susi*, 58 CCPA 1074, 1079-80, 169 USPQ 423, 426 (C.C.P.A. 1971)(relating to light stable polymers); *In re Crockett*, 279 F.2d 274, 276-277, 126 USPQ 186, 188 (C.C.P.A. 1960)(relating to use of magnesium oxide and calcium carbide in cast iron). Thus, Appellant maintains that the pharmaceutical arts, and in particular anti-cancer treatments, are very unpredictable.

In the Advisory Action dated July 28, 2004, the Examiner responds to the Appellant's inquiry regarding the previous statements about FDA approval by stating "Applicant asks why the Examiner says that the plant extracts do not need FDA approval. This is because they are natural products, i.e., they are not synthetically made. Thus, there is nothing unpredictable about them". (Page 3)

Appellant does not understand why the Examiner asserts that synthetic compounds are more unpredictable than products of nature. What is unpredictable about oridonin and lupulone is their mechanism of action, not the compounds themselves. Whether the compounds are of synthetic or natural origin, the motivation to combine the compounds comes not from a general disclosure of anticancer activity, but from detailed studies of the mechanism of the compounds as performed by the Appellant. Regardless of the origin of oridonin and lupulone, the prior art does not teach that the compounds can be used to treat the same types of cancers, or that they operate by the same mechanism and thus should not have antagonistic effects. The mere fact that the compounds are natural products has nothing to do with the predictability of their biological mechanism.

In summary, Appellant has clearly shown that oridonin and lupulone an be used to treat breast and prostate cancer. In addition, because oridonin and lupulone are both cell cycle inhibitors, they are not expected to have antagonistic effects. The cited references provide neither the motivation nor the expectation of success for this combination. Appellant submits that the present claims are patentable over the prior art.

IX. CONCLUSION:

In view of the foregoing, it is urged that the final rejection of Claims 1-9, 11-16, 18-23, 26-29, and 32-35 be overturned and the Claims allowed. The final rejection is in error and should be reversed.

If there are any additional charges with respect to this Brief, please charge them to Deposit Account No. 06-1130.

Respectfully submitted,

CANTOR COLBURN, LLP

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Appendix 1:

1. A composition for treating or preventing prostate cancer or breast cancer:

oridonin, a pharmaceutically acceptable salt or ester of oridonin, a selectively substituted analog of oridonin, or a combination thereof; and

lupulone, a pharmaceutically acceptable salt or ester of lupulone, a selectively substituted analog of lupulone, or a combination thereof;

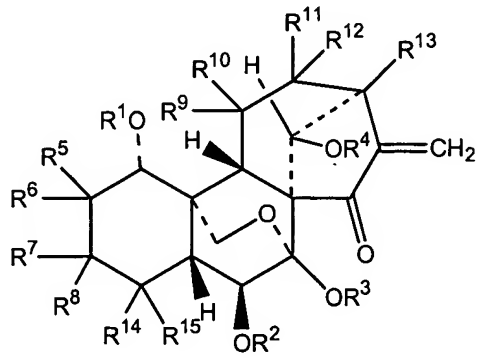
wherein the composition is suitable for the treatment or prevention of prostate cancer or breast cancer.

2. The composition of Claim 1, in an ingestible form.

3. The composition of Claim 2, wherein the ingestible form is a powder, a capsule, or a tablet.

4. The composition of Claim 1, in the form of a suppository.

5. The composition of Claim 1, comprising a compound having the structure



wherein R^1-R^4 are each independently hydrogen, C_1-C_6 alkyl, or C_1-C_{12} acyl, R^5-R^{13} are each independently hydrogen or C_1-C_6 alkyl, and R^{14} and R^{15} are each independently C_1-C_6 alkyl, with the proviso that at least 4 of R^5-R^{13} are hydrogen.

6. The composition of Claim 5, wherein R^1-R^4 are each independently hydrogen, methyl, ethyl, acetyl, or propionyl.

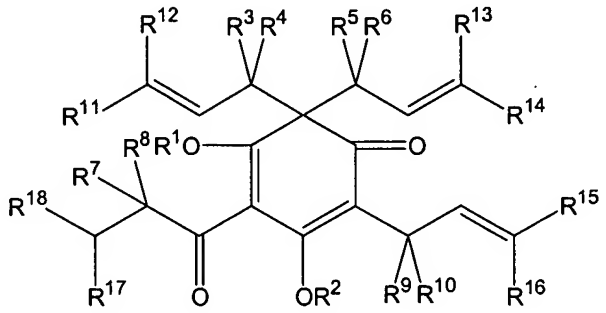
7. The composition of Claim 5, wherein R^5-R^{13} are each independently hydrogen, methyl, or ethyl.

8. The composition of Claim 5, wherein R^1-R^{13} are hydrogen, and R^{14} and R^{15} are methyl.

9. The composition of Claim 5, comprising an extract of Rabdosia rubescens.

10. (canceled)

11. The composition of Claim 1, comprising a compound having the structure



wherein R^1 and R^2 are each independently hydrogen, C_1-C_6 alkyl, or C_1-C_{12} acyl; R^3-R^{10} are each independently hydrogen or C_1-C_6 alkyl with the proviso that at least four of R^3-R^{10} are hydrogen; and R^{11}-R^{18} are each independently C_1-C_6 alkyl.

12. The composition of Claim 11, wherein R^1 and R^2 are each independently hydrogen, methyl, ethyl, acetyl, or propionyl.

13. The composition of Claim 11, wherein R^3-R^{10} are each independently hydrogen, methyl, or ethyl.

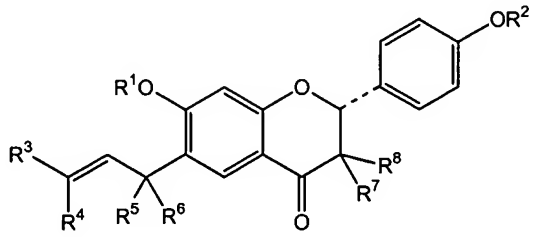
14. The composition of Claim 11, wherein R^{11}-R^{18} are each independently methyl or ethyl.

15. The composition of Claim 11, wherein R^1-R^{10} are each hydrogen, and R^{11}-R^{18} are each methyl.

16. The composition of Claim 11, comprising an extract of Humulus lupulus.

17. (canceled)

18. The composition of Claim 1, comprising a compound having the structure



wherein R^1 and R^2 are each independently hydrogen, C_1-C_6 alkyl, or C_1-C_{12} acyl; and R^3-R^8 are each independently hydrogen or C_1-C_6 alkyl with the proviso that at least two of R^3-R^8 are hydrogen.

19. The composition of Claim 18, wherein R^1 and R^2 are each independently hydrogen, methyl, ethyl, acetyl, or propionyl.

20. The composition of Claim 18, wherein R^3-R^8 are each independently hydrogen, methyl, or ethyl.

21. The composition of Claim 18, wherein R^3 and R^4 are methyl.

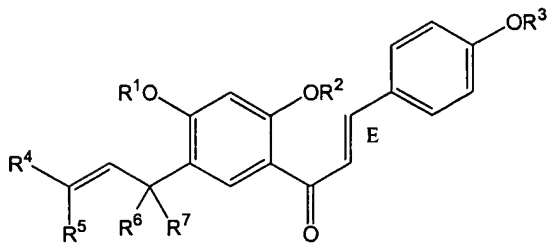
22. The composition of Claim 18, wherein R^1, R^2, and R^5-R^8 are hydrogen; and R^3 and R^4 are methyl.

23. The composition of Claim 18, wherein R^2 and R^5-R^8 are hydrogen; and R^1, R^3, and R^4 are methyl.

24. (canceled)

25. (canceled)

26. The composition of Claim 1, comprising a compound having the formula



wherein R^1-R^3 are each independently hydrogen, C_1-C_6 alkyl, or C_1-C_{12} acyl; and R^4-R^7 are each independently hydrogen or C_1-C_6 alkyl.

27. The composition of Claim 26, wherein R^1-R^3 are each independently hydrogen, methyl, ethyl, acetyl, or propionyl.

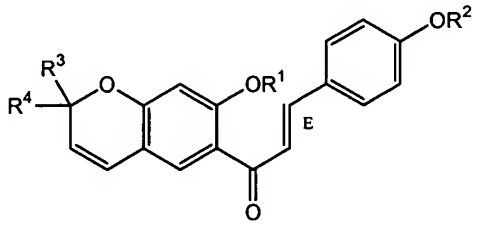
28. The composition of Claim 26, wherein R^4-R^7 are each independently hydrogen, methyl, or ethyl.

29. The composition of Claim 26, wherein R^1-R^3, R^6, and R^7 are hydrogen; and R^4 and R^5 are methyl.

30. (canceled)

31. (canceled)

32. The composition of Claim 1, comprising a compound having the structure



wherein R^1 and R^2 are each independently hydrogen, C_1-C_6 alkyl, or C_1-C_{12} acyl; and R^3 and R^4 are each independently hydrogen or C_1-C_6 alkyl.

33. The composition of Claim 32, wherein R^1 and R^2 are each independently hydrogen, methyl, ethyl, acetyl, or propionyl.

34. The composition of Claim 32, wherein R^3 and R^4 are each independently hydrogen, methyl, or ethyl.

35. The composition of Claim 32, wherein R^1 and R^2 are hydrogen; and R^3 and R^4 are methyl.

36-48. (canceled)